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## A STEREOCONTROLLED SYNTHESIS OF ( $\pm$ )- $\beta$ -ISOSPARTEINE

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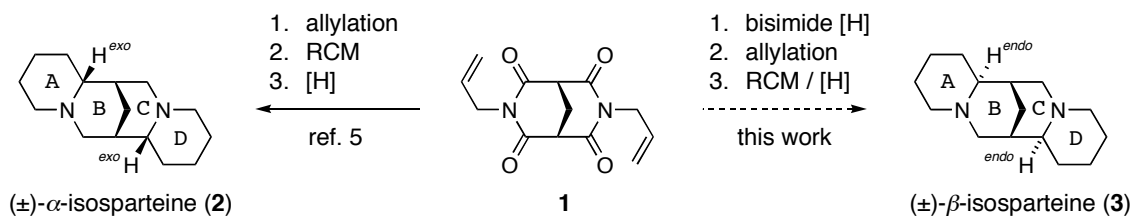
**Abstract** – A versatile tetraoxobispidine synthon, 3,7-diallyl-2,4,6,8-tetraoxo-3,7-diazabicyclo[3.3.1]nonane (**1**), was converted to the title alkaloid via a synthetic sequence incorporating: imide reduction, Sakurai allylation, and ring-closing olefin metathesis reactions.

## INTRODUCTION<sup>†</sup>

Widespread among common papilionaceous plant species, the sparteine family of quinolizidine alkaloids are constituted by all geometrically possible stereoisomeric variations of the 3,11-diazatetracyclo-[7.7.1.0<sup>3,8</sup>.0<sup>11,16</sup>]heptadecane nucleus.<sup>1</sup> Though of relatively minor biological importance,<sup>2</sup> sparteine alkaloids, and in particular, (–)-sparteine and (–)- $\alpha$ -isoparteine, have elicited intense interest because of their status as chiral diamine ligands *par excellence* for metal mediated enantioselective synthesis.<sup>3,4</sup> In an earlier report,<sup>5</sup> we identified that tetraoxobispidine derivatives may provide a versatile synthetic platform for the elaboration of all members of the sparteine alkaloid group.<sup>6</sup> In support of this modest hypothesis, we successfully demonstrated the conversion of *N,N'*-diallyltetraoxobispidine (**1**) to ( $\pm$ )- $\alpha$ -isoparteine (**2**). To ensure brevity of execution, our synthesis of **2** relied on two-directional advancement from **1** and proceeded *via* double nucleophilic allylation, followed by double ring-closing olefin metathesis (RCM) and thence exhaustive reduction to yield the target (Scheme 1).<sup>5</sup> In principle, a synthesis along similar lines in which the order of introduction of allyl and hydride nucleophiles onto **1** was strategically reversed, would result in endo configured ring junction hydrogen-atoms and ultimately afford ( $\pm$ )- $\beta$ -isoparteine (**3**).<sup>7</sup> This lesser known member of the sparteine subgroup of lupine alkaloids

<sup>†</sup> Dedicated to Prof. Steven M. Weinreb on the occasion of his 65th birthday.

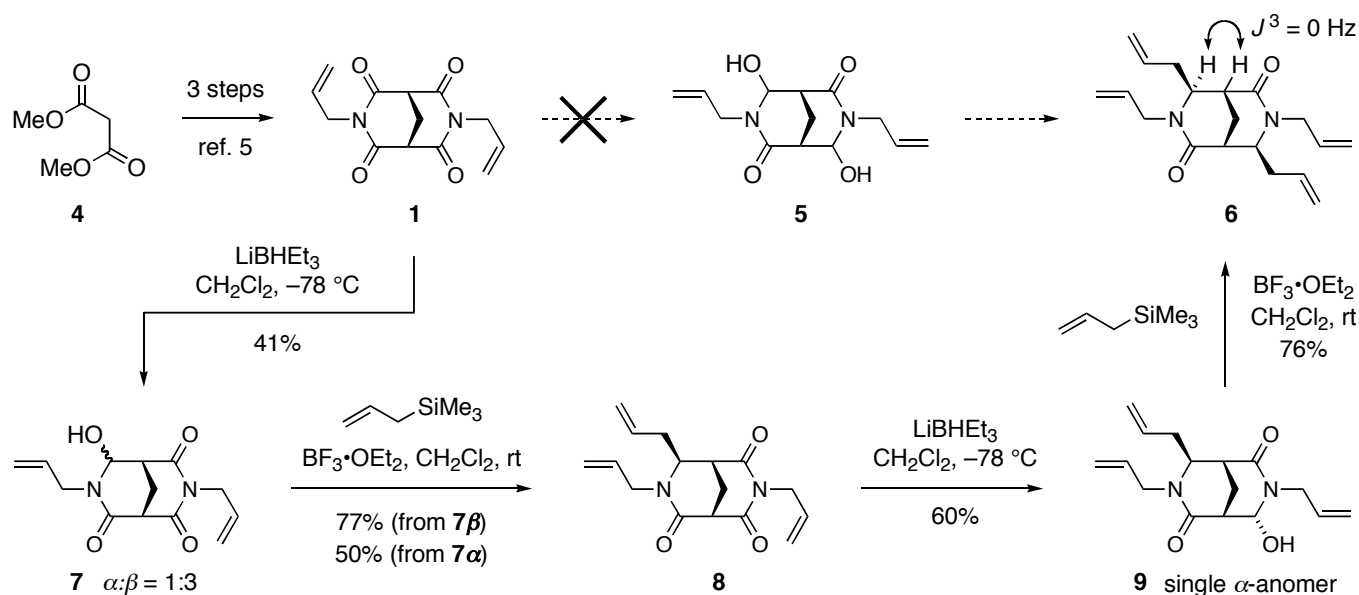
has received comparatively little attention and has never been the focus of a stereocontrolled target directed synthesis.<sup>8</sup> Herein, we advance such an undertaking and describe the successful elaboration of ( $\pm$ )- $\beta$ -isosparteine (**3**) from readily available synthon (**1**).



**Scheme 1.** Overview of synthetic strategy for planned assault on ( $\pm$ )- $\beta$ -isosparteine (**3**).

## RESULTS AND DISCUSSION

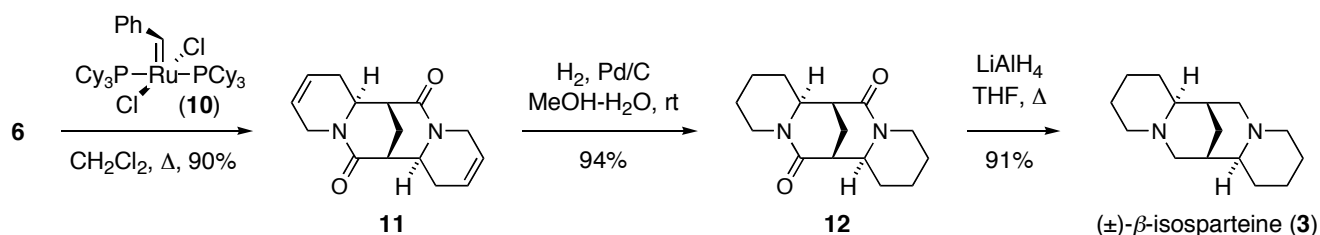
Synthesis of ( $\pm$ )- $\beta$ -isosparteine commenced from tetraoxobispidine (**1**), itself prepared in short order from dimethyl malonate (**4**) as previously described (Scheme 2).<sup>5</sup> In keeping with the efficient two-directional approach of our earlier  $\alpha$ -isosparteine synthesis, we planned to access  $\beta$ -isosparteine precursor (**6**) from bicycle (**1**) via a two step reductive allylation sequence comprising regioselective double hydride addition followed by double Sakurai-type allylation of the resulting bishemiaminal (**5**). In the event, and in spite of our best efforts, it proved impossible to prepare **5** from **1** in the desired manner. To obviate difficulties associated with the production and handling of a potentially sensitive bishemiaminal, a less direct route to **6** which avoided such an intermediate altogether was next investigated.



**Scheme 2.** Net double reductive regioselective *exo*-face allylation of tetraoxobispidine (**1**).

After some experimentation, it was discovered that bisimide (**1**) could be successfully monoreduced, albeit in modest yield, by the action of lithium triethylborohydride.<sup>9</sup> Subjection of either anomer of the resulting hemiaminal (**7**)<sup>10</sup> to a Sakurai-type allylation reaction gave allyl addition product (**8**) as a single

isomer.<sup>11,12</sup> Repetition of the same two step reduction/allylation sequence from **8** proceeded in a remarkably regio- and stereoselective fashion to afford tetraene (**6**), an appropriate RCM precursor to the  $\beta$ -isosparteine ring system. The  $C_2$ -symmetric nature of **6** was clearly evident from its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral signatures; furthermore, the absence of  $J$ -coupling between vicinal bridgehead and CHN methine protons within **6** indicated the expected *exo*-configurations for the newly introduced pair of allyl moieties.<sup>13</sup> Subsequent conversion of tetraene (**6**) to the target of ultimate interest was uneventful (Scheme 3). Thus, treatment of **6** with Grubbs' first generation metathesis catalyst (**10**),<sup>14</sup> gave the expected tetracyclic product (**11**) in 90% yield. Adjustment of the oxidation level of **11** *via* hydrogenation followed by reduction of the resulting ( $\pm$ )-10,17-dioxo- $\beta$ -isosparteine (**12**)<sup>15</sup> with lithium aluminum hydride gave ( $\pm$ )- $\beta$ -isosparteine (**3**) as a colorless oil. The synthetic sample of ( $\pm$ )-**3** so produced exhibited identical  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectral data to those previously reported for this alkaloid in the literature.<sup>8b,16</sup>



**Scheme 3.** Completion of synthesis of ( $\pm$ )- $\beta$ -isosparteine (**3**).

In summary, ( $\pm$ )- $\beta$ -isosparteine (**3**) was synthesized in seven steps from *N,N'*-diallyltetraoxobispidine (**1**) *via* strategic application of reduction, Sakurai, and RCM transformations. This work serves to further exemplify the inherent versatility of the tetraoxobispidine approach to the stereocontrolled synthesis of sparteine group alkaloids. Studies directed at the realization of enantioselective nucleophilic additions to tetraoxobispidine platforms are ongoing as are allied efforts to conclude a synthesis of the eponymous sparteine group alkaloid from **1**. This work will be reported in due course.

## EXPERIMENTAL

**General techniques:** All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under an atmosphere of  $\text{N}_2$ . Prior to use, THF was freshly distilled from sodium benzophenone ketyl and  $\text{CH}_2\text{Cl}_2$  was distilled from  $\text{CaH}_2$ . Preparative chromatographic separations were performed on silica gel 60 (35–75  $\mu\text{m}$ ) and reactions followed by TLC analysis using silica gel 60 plates (2–25  $\mu\text{m}$ ) with fluorescent indicator (254 nm) and visualized with UV or phosphomolybdic acid. All commercially available reagents were used as received unless otherwise noted. Melting points were determined from open capillary tubes on a melting point apparatus and are uncorrected. Infra-red spectra were recorded in Fourier transform mode from KBr disks for solids, and as a thin film supported between NaCl plates for

oils.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded in Fourier transform mode at the field strength specified and from the indicated deuterated solvents in standard 5 mm diameter tubes. Chemical shift in ppm is quoted relative to residual solvent signals calibrated as follows:  $\text{CDCl}_3$   $\delta_{\text{H}}$  ( $\text{CHCl}_3$ ) = 7.26 ppm,  $\delta_{\text{C}}$  = 77.2 ppm. Multiplicities in the  $^1\text{H}$  NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Numbers in parentheses following carbon atom chemical shifts refer to the number of attached hydrogen atoms as revealed by the DEPT spectral editing technique. Low (MS) and high resolution (HRMS) mass spectra were obtained using electrospray (ES) ionization. Ion mass/charge ( $m/z$ ) ratios are reported as values in atomic mass units.

**( $\pm$ )-(1*R*/\*,5*S*\*,6*R*\*)-3,7-Diallyl-6-hydroxy-2,4,8-trioxo-3,7-diazabicyclo[3.3.1]nonane (7):** A stirred solution of bisimide (**1**, 3.50 g, 13.4 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (45 mL) at  $-78^\circ\text{C}$  under  $\text{N}_2$ , was treated dropwise with lithium triethylborohydride (14.7 mL, 1.0 M in THF, 14.7 mmol) during 20 min. The resulting mixture was stirred for 1 h at  $-78^\circ\text{C}$  and then quenched with sat. aq.  $\text{NH}_4\text{Cl}$  (10 mL) and warmed to rt. Further  $\text{H}_2\text{O}$  (10 mL) and  $\text{CH}_2\text{Cl}_2$  (20 mL) were added and the layers well shaken and separated. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (2x15 mL) and the combined organic phases dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluting with 1% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield a mixture of hemiaminal anomers (**7**, 1.46 g, 5.53 mmol, 41%,  $\alpha:\beta$  = 1:3) as a colorless oil. A sample of pure  $\beta$ -isomer (**7 $\beta$** ) was isolated as a colorless solid by careful chromatography. Data for **7 $\beta$** : mp  $94\text{--}98^\circ\text{C}$  (*t*-BuOMe); IR (KBr) 3380, 2978, 1736, 1669, 1455, 1272, 1206, 1059, 929, 760, 554  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.75 (2H, ddt,  $J$  = 16.7, 10.3, 6.5 Hz), 5.22 (1H, bs), 5.21 (1H, dm,  $J$  = 10.2 Hz), 5.18 (1H, dm,  $J$  = 16.3 Hz), 5.14 (1H, dm,  $J$  = 10.1 Hz), 5.12 (1H, dm,  $J$  = 15.8 Hz), 4.39–4.28 (3H, m), 3.85 (1H, ddm,  $J$  = 14.8, 6.6 Hz), 3.75 (1H, q,  $J$  = 2.6 Hz), 3.35 (1H, d,  $J$  = 5.1 Hz), 3.26 (1H, dq,  $J$  = 4.4, 2.1 Hz), 2.77 (1H, ddd,  $J$  = 13.7, 3.4, 2.1 Hz), 2.29 (1H, dddd,  $J$  = 13.6, 3.7, 2.3, 1.1 Hz) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.5 (0), 167.7 (0), 163.7 (0), 132.4 (1), 131.2 (1), 119.0 (2), 118.2 (2), 80.1 (1), 48.8 (1), 47.1 (2), 45.2 (1), 42.0 (2), 19.6 (2) ppm; MS (ES)  $m/z$  265 ( $\text{M}+\text{H}$ ) $^+$ ; HRMS (ES)  $m/z$  287.1003 (calcd. for  $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_4\text{Na}$ : 287.1008).

**( $\pm$ )-(1*R*\*,5*S*\*,6*R*\*)-3,6,7-Triallyl-2,4,8-trioxo-3,7-diazabicyclo[3.3.1]nonane (8):** A stirred solution of isomerically pure hemiaminal (**7 $\beta$** , 459 mg, 1.74 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (6 mL) at rt under  $\text{N}_2$ , was treated sequentially in dropwise fashion with allyltrimethylsilane (2.75 mL,  $d$  = 0.72, 1.98 g, 17.3 mmol) followed by freshly distilled boron trifluoride diethyl etherate (1.07 mL,  $d$  = 1.13, 1.21 g, 8.52 mmol). The resulting yellow mixture was stirred at rt for 24 h. After this time,  $\text{CH}_2\text{Cl}_2$  (20 mL) was added and the mixture washed with  $\text{H}_2\text{O}$  (2x5 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluting with 1% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield triallyl compound (**8**, 384 mg, 1.33 mmol, 77%) as a colorless oil. A comparable reaction from **7 $\alpha$**  (127 mg, 0.48 mmol,  $\alpha:\beta$  = 5:1) gave an identical product (**8**, 69 mg, 0.24 mmol, 50%). Data for **8**: IR (neat) 3453, 3082, 2950, 1737,

1684, 1651, 1454, 1417, 1356, 1330, 1275, 1228, 1191, 1122, 993, 925, 843, 731, 627, 553, 499  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.79-5.70 (2H, m), 5.64 (1H, dddd,  $J = 17.1, 10.2, 7.8, 4.9$  Hz), 5.27-5.10 (6H, m), 4.55 (1H, ddt,  $J = 15.2, 5.0, 1.4$  Hz), 4.37 (1H, ddt,  $J = 14.6, 5.8, 1.4$  Hz), 4.32 (1H, ddt,  $J = 14.6, 5.8, 1.4$  Hz), 3.73 (1H, dd,  $J = 9.6, 3.5$  Hz), 3.70-3.68 (1H, m), 3.52 (1H, dd,  $J = 15.2, 7.4$  Hz), 3.17-3.13 (1H, m), 2.73 (1H, dm,  $J = 7.1$  Hz), 2.39 (1H, ddd,  $J = 12.6, 3.4, 2.1$  Hz), 2.30-2.22 (2H, m) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  173.1 (0), 168.1 (0), 162.9 (0), 132.8 (1), 132.0 (1), 131.4 (1), 120.0 (2), 119.0 (2), 118.2 (2), 58.6 (1), 48.2 (1), 47.8 (2), 42.0 (2), 39.8 (1), 36.7 (2), 19.7 (2) ppm; MS (ES)  $m/z$  288  $\text{M}^+$ ; HRMS (ES)  $m/z$  288.1471 (calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_3$ : 288.1474).

**( $\pm$ )-(1*R*\*,4*R*\*,5*R*\*,8*S*\*)-2,6-Dioxo-4-hydroxy-3,7,8-triallyl-3,7-diazabicyclo[3.3.1]nonane (9):** A stirred solution of imide (**8**, 69 mg, 0.240 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (2 mL) at  $-78^\circ\text{C}$  under  $\text{N}_2$ , was treated dropwise with lithium triethylborohydride (0.29 mL, 1.0 M in THF, 0.29 mmol) during 2 min. The resulting mixture was stirred for 1 h at  $-78^\circ\text{C}$  and then quenched with sat. aq. potassium sodium tartrate (5 mL) and warmed to rt.  $\text{H}_2\text{O}$  (10 mL) and EtOAc (10 mL) were added and the layers well shaken and separated. The aqueous layer was extracted with EtOAc (2x5 mL) and the combined organic phases dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluting with 5% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield hemiaminal (**9**, 42 mg, 0.145 mmol, 60%, single  $\alpha$ -anomer) as a colorless oil: IR (neat) 3389, 3080, 2926, 1622, 1452, 1356, 1280, 1179, 1072, 985, 924  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.84-5.58 (3H, m), 5.20-5.12 (5H, m), 5.09 (1H, dq,  $J = 11.7, 1.3$  Hz), 5.01 (1H, dd,  $J = 10.0, 4.4$  Hz), 4.84 (1H, d,  $J = 10.0$  Hz), 4.40 (1H, ddt,  $J = 15.4, 4.8, 1.7$  Hz), 4.22 (1H, ddt,  $J = 14.8, 5.0, 1.4$  Hz), 4.01 (1H, ddm,  $J = 14.8, 7.1$  Hz), 3.69-3.59 (2H, m), 2.99-2.93 (1H, m), 2.82 (1H, dq,  $J = 4.3, 2.1$  Hz), 2.66 (1H, dddt,  $J = 14.6, 5.6, 4.1, 1.5$  Hz), 2.32-2.19 (2H, m), 1.87 (1H, ddm,  $J = 13.8, 4.4$  Hz) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0 (0), 168.7 (0), 133.2 (1), 133.1 (1), 131.7 (1), 119.4 (2), 118.3 (2), 117.7 (2), 81.1 (1), 58.6 (1), 48.0 (2), 43.8 (2), 41.4 (1), 39.7 (1), 36.5 (2), 19.0 (2) ppm; MS (ES)  $m/z$  313 ( $\text{M}+\text{Na}$ ) $^+$ ; HRMS (ES)  $m/z$  313.1518 (calcd. for  $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}_3\text{Na}$ : 313.1523).

**( $\pm$ )-(1*R*\*,4*S*\*,5*R*\*,8*S*\*)-2,6-Dioxo-3,4,7,8-tetraallyl-3,7-diazabicyclo[3.3.1]nonane (6):** A stirred solution of hemiaminal (**9**, 68 mg, 0.234 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (1 mL) at rt under  $\text{N}_2$ , was treated sequentially in dropwise fashion with allyltrimethylsilane (0.36 mL,  $d = 0.72$ , 259 mg, 2.27 mmol) followed by freshly distilled boron trifluoride diethyl etherate (0.15 mL,  $d = 1.13$ , 170 mg, 1.20 mmol). The resulting mixture was stirred at rt for 24 h. After this time,  $\text{CH}_2\text{Cl}_2$  (20 mL) was added and the mixture washed with  $\text{H}_2\text{O}$  (2x5 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluting with 1% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield tetraene (**6**, 56 mg, 0.178 mmol, 76%) as a colorless solid: mp  $97-99^\circ\text{C}$  (hexanes); IR (KBr) 2976, 1634, 1455, 1416, 1355, 1279, 1242, 1191, 1138, 1114, 1077, 1053, 998, 978, 956, 926, 842, 736, 712  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.80-5.64 (4H, m), 5.19-5.11 (8H, m), 4.43 (2H, dd,  $J = 15.2, 5.1$  Hz), 3.67 (2H, dd,  $J = 10.4, 3.6$  Hz),

3.54 (2H, dd,  $J = 15.1, 7.1$  Hz), 2.78 (2H, t,  $J = 3.0$  Hz), 2.64 (2H, dddt,  $J = 14.5, 5.3, 3.9, 1.4$  Hz), 2.22 (2H, dt,  $J = 14.4, 9.4$  Hz) 2.08 (2H, t,  $J = 3.0$  Hz) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.5 (2C, 0), 133.6 (2C, 1), 132.6 (2C, 1), 119.0 (2C, 2), 118.2 (2C, 2), 59.8 (2C, 1), 47.7 (2C, 2), 39.3 (2C, 1), 36.4 (2C, 2), 16.4 (2) ppm; MS (ES)  $m/z$  315 ( $\text{M}+\text{H}$ ) $^+$ ; HRMS (ES)  $m/z$  315.2061 (calcd. for  $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_2$ : 315.2067).

**( $\pm$ )- $\Delta^{3,13}$ -Didehydro-10,17-dioxo- $\beta$ -isosparteine (11):** A stirred solution of tetraene (**6**, 41 mg, 0.131 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.5 mL) at rt under  $\text{N}_2$ , was treated with Grubbs' 1st generation catalyst (**10**, 11 mg, 0.013 mmol) $^{14}$  in one portion. The resulting mixture was heated to a gentle reflux for 16 h, cooled to rt, and concentrated *in vacuo*. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluting with 1% MeOH in  $\text{CH}_2\text{Cl}_2$ ) to yield tetracycle (**11**, 30 mg, 0.12 mmol, 90%) as a colorless solid: mp 195-197 °C (hexanes-EtOAc); IR (KBr) 2915, 1636, 1455, 1356, 1250, 1147, 959, 674, 661  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.84-5.78 (2H, m), 5.72-5.67 (2H, m), 4.82 (2H, bd,  $J = 18.4$  Hz), 3.84 (2H, dd,  $J = 11.4, 3.6$  Hz), 3.46 (2H, bd,  $J = 18.4$  Hz), 2.70 (2H, t,  $J = 2.7$  Hz), 2.40 (2H, bt,  $J = 14.4$  Hz), 2.18 (2H, bd,  $J = 16.8$  Hz), 2.13 (2H, t,  $J = 2.9$  Hz) ppm;  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  169.6 (2C, 0), 124.6 (2C, 1), 124.3 (2C, 1), 56.2 (2C, 1), 42.8 (2C, 2), 41.5 (2C, 1), 31.6 (2C, 2), 17.4 (2) ppm; MS (ES)  $m/z$  281 ( $\text{M}+\text{Na}$ ) $^+$ ; HRMS (ES)  $m/z$  281.1249 (calcd. for  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}$ : 281.1260).

**( $\pm$ )-10,17-Dioxo- $\beta$ -isosparteine (12):** A suspension of diene (**11**, 20 mg, 0.078 mmol) and 10 wt.% Pd/C (2 mg) in MeOH- $\text{H}_2\text{O}$  (2:1, 1.5 mL) was stirred vigorously under an atmosphere of  $\text{H}_2$  gas for 7 h. After this time, the active gas was purged with inert gas ( $\text{N}_2$ ) and the reaction mixture filtered through a celite pad. The pad was washed with  $\text{CH}_2\text{Cl}_2$  (2x20 mL) and the filtrate and combined washings concentrated *in vacuo* to yield ( $\pm$ )-10,17-dioxo- $\beta$ -isosparteine (**12**, 19 mg, 0.073 mmol, 94%) as a colorless solid: mp 172-174 °C (hexanes-Et $_2\text{O}$ ); IR (KBr) 2928, 2851, 1627, 1459, 1436, 1358, 1269, 1236, 1201, 1143, 1055, 1011, 898, 856, 755, 572, 562  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.70 (2H, dm,  $J = 12.9$  Hz), 3.52 (2H, dm,  $J = 11.3$  Hz), 2.58 (2H, t,  $J = 2.9$  Hz), 2.45 (2H, td,  $J = 12.8, 2.5$  Hz), 2.10 (2H, t,  $J = 3.0$  Hz), 1.97-1.92 (2H, m), 1.75-1.52 (8H, m), 1.48-1.34 (2H, m);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  169.2 (2C, 0), 60.6 (2C, 1), 43.6 (2C, 2), 42.7 (2C, 1), 32.3 (2C, 2), 25.4 (2C, 2), 25.0 (2C, 2), 18.9 (2) ppm; MS (ES)  $m/z$  263 ( $\text{M}+\text{H}$ ) $^+$ ; HRMS (ES)  $m/z$  263.1746 (calcd. for  $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_2$ : 263.1754).

**( $\pm$ )- $\beta$ -Isosparteine (3):** Protocol taken from O'Brien's synthesis of (–)-sparteine. $^{4e}$  A stirred solution of bislactam (**12**, 21 mg, 0.080 mmol) in anhydrous THF (0.5 mL) at 0 °C under  $\text{N}_2$ , was treated with excess lithium aluminum hydride (37 mg, 0.97 mmol) and the resulting suspension heated at reflux for 13 h. The mixture was then cooled, diluted with Et $_2\text{O}$  (5 mL), and quenched by the careful addition of hydrated  $\text{Na}_2\text{SO}_4$  (100 mg). After vigorous stirring for 30 min, the mixture was filtered through a celite pad and the residue washed well with 10% MeOH in  $\text{CH}_2\text{Cl}_2$  (20 mL). The filtrate and combined washings were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo* to afford essentially pure ( $\pm$ )- $\beta$ -isosparteine (**3**, 17 mg, 0.073, 91%) as a colorless oil: IR (neat) 3420 ( $\text{H}_2\text{O}$ ), 2926, 1643, 1443, 1298, 1221, 1129  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,

CDCl<sub>3</sub>)  $\delta$  3.01 (2H, dd,  $J$  = 10.8, 6.6 Hz), 2.79 (2H, dm,  $J$  = 12.6 Hz), 2.44 (2H, td,  $J$  = 12.7, 2.8 Hz), 2.25 (2H, dm,  $J$  = 11.7 Hz), 2.16 (2H, dd,  $J$  = 10.8, 3.0 Hz), 1.81-1.72 (2H, m), 1.70-1.48 (8H, m), 1.45-1.20 (6H, m) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  63.0 (2C, 1), 55.3 (2C, 2), 55.1 (2C, 2), 34.6 (2C, 1), 28.8 (2C, 2), 25.6 (2C, 2), 22.8 (2C, 2), 20.0 (2) ppm; MS (ES)  $m/z$  235 (M+H)<sup>+</sup>, 159; HRMS (ES)  $m/z$  235.2164 (calcd. for C<sub>15</sub>H<sub>27</sub>N<sub>2</sub>: 235.2169). <sup>1</sup>H and <sup>13</sup>C NMR data are in agreement with those reported by Wanner and Koomen.<sup>8b</sup> <sup>13</sup>C NMR data are also in agreement with those reported by Galasso *et al.*<sup>16</sup>

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